Assessing Oximetry Response to Chimeric Antigen Receptor T-cell Therapy against Glioma with (19)F MRI in a Murine Model.

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Public Summary:
To assess the cell-specific, intracellular partial pressure of oxygen (Po2) dynamics of both tumor and chimeric antigen receptor (CAR) T cells in a murine immunotherapy model.

Scientific Abstract:
Purpose: To assess the cell-specific, intracellular partial pressure of oxygen (Po2) dynamics of both tumor and chimeric antigen receptor (CAR) T cells in a murine immunotherapy model. Materials and Methods: Human glioblastoma cells or human T cells were intracellularly labeled with perfluorocarbon nanoemulsion droplet sensors prior to in vivo injection in severe combined immunodeficient mice to measure Po2 in the two cell types in response to treatment. Two main sets of experiments were performed: (a) mice were injected in the flank with perfluorocarbon-labeled human glioblastoma cells and were then inoculated with either CAR T cells or untransduced T cells or were untreated 5 days after tumor inoculation; and (b) mice with unlabeled glioblastoma tumors were inoculated with perfluorocarbon-labeled CAR T cells or untransduced T cells 5 days after tumor inoculation. Longitudinal fluorine 19 ((19)F) spin-lattice relaxation time measurements of the tumor mass were used to ascertain absolute Po2 in vivo. Results were analyzed for significance using an analysis of variance, a linear mixed-effect model, and a Pearson correlation coefficient test, as appropriate. Results: The intracellular tumor cell Po2 temporal dynamics exhibited delayed, transient hyperoxia at 3 days after infusion of CAR T cells, commensurate with significant tumor cell killing and CAR T-cell infiltration, as observed by bioluminescence imaging and histologic findings. Conversely, no significant changes were detected in CAR or untransduced T-cell intracellular Po2 over time in tumor using these same methods. Moreover, it was observed that the total (19)F tumor cell signal quenches with treatment, consistent with rapid tissue clearance of probe from apoptotic tumor cells. Conclusion: Cell-specific Po2 measurements using perfluorocarbon probes can provide insights into effector cell function and tumor response in cellular immunotherapeutic cancer models.Keywords: Animal Studies, MR-Imaging, MR-Spectroscopy, Molecular Imaging-Cancer, Molecular Imaging-Immunotherapy Supplemental material is available for this article. (c) RSNA, 2021See also commentary by Bulte in this issue.